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EXAMINER

HUI, SAN MING R

ART UNIT PAPER NUMBER

1617

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/982,554
Filing Date: October 18, 2001
Appellant(s): ZOHOUNGBOGBO, MATHIAS C.

Robert Haroun
317 Madison Avenue, Suite 910
New York, New York 10017
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 6, 2005.

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(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The amendment after final rejection filed on June 6, 2005 has been entered.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

The rejection of claims 45-56 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

Marquie et al., Life Sciences, 1998;63(1):65-76

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Pentikainen et al., Annals of Medicine, 1990;22:307-312

Poupon et al., Hepatology, 1993;17(4):577-582

Spasmo-canulase(r) Bitab(r) package insert, July 1989

Krause et al., Food, Nutrition, and Therapy, 7th ed., 1984, pages 656-658, W.B.

Saunders Company

Hydrocotyle - A modern Herbal Home Page, 1995

Kang et al., Archives of Physiology and Biochemistry, 1997;105(6):603-607

Pondimin monograph from PDR, 1996, page 2066-2067

WO95/11034

Keown et al.

4-1995

(10) Grounds of Rejection

The outstanding rejections under 35 USC 112 are withdrawn in view of the amendments filed June 6, 2005.

The outstanding objection is withdrawn in view of the amendments filed June 6, 2005.

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 45, 47, 49-50, 52, and 54 -56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marquie et al. (Life Sciences, 1998; 63(1):65-76), Pentikainen et al. (Annals of Medicine, 1990 ;22 :307-312), and Poupon et al. (Hepatology, 1993; 17(4): 577-582) in view of Spasmo-canalase® Bitab® package insert (July 1989), references of record and Krause et al., (Food, Nutrition, and Therapy, 7th ed., 1984, page 656-658, W.B. Saunders Company).

Marquie et al. teaches benfluorex as useful in treating hypercholesterolemia (See abstract, also page 74, whole page).

Pentikain et al. teaches the cholesterol lowering affect of metformin (See the abstract, also page 309, Table 2).

Poupon et al. teaches ursodesoxycholic acid as useful in lowering hypercholesterolemia (See particularly the abstract).

The references do not expressly teach the method of treating the side effects of a ketogenic diet with the combination of benfluorex, metformin and ursodesoxycholic acid. The references do not expressly teach the herein claimed amount ratio employed. The references do not expressly teach the employment of pancreatin and sodium

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dehydrocholate with benfluorex and metformin. The references do not expressly teach the dosage of the composition herein claimed as 7g to 23g. The references do not expressly teach the method further include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine whether the patients is suffering from the side effects of ketogenic diet.

Spasmo-canulase[®] Bitab[®] package insert teaches Spasmo-canulase[®] Bitab[®], which contains pancreatin and sodium dehydrocholate, is useful in treating abdominal camps associated with flatulence.

Krause et al. teaches ketogenic diet as approximately 90% of calories are from fat and only around 11% of calories are from proteins and carbohydrates (page 657, col. 1-2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat side effects of a ketogenic diet (hypercholesterolemia being one of the side effects of ketogenic diet) with the combination of benfluorex, metformin and ursodesoxycholic acid. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate pancreatin and sodium dehydrocholate in the treatment method herein. It would have been obvious to one of ordinary skill in the art at the time the invention was made to include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine whether the patients is suffering from the side effects of ketogenic diet.

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One of ordinary skill in the art would have been motivated to treat side effects of a ketogenic diet (hypercholesterolemia being one of the side effects of ketogenic diet) with the combination of benfluorex, metformin and ursodesoxycholic acid. Combining and employing two or more agents which are known to be useful to lowering hypercholesterolemia individually into a single method useful for the very same purpose (treating hypercholesterolemia) is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. One of ordinary skill in the art would have been motivated to incorporate pancreatin and sodium dehydrocholate in the treatment method herein because Spasmo-canulase® Bitab®, which contains pancreatin and sodium dehydrocholate, is known for relieving abdominal cramps associated with flatulence. Since flatulence and abdominal cramps are the common side effects of metformin, employing Spasmo-canulase® Bitab® would be reasonably expected to be effective in relieving the side effects of metformin and be useful in the herein claimed method, which utilize metformin. Furthermore, the optimization of result effect parameters (i.e., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

One of ordinary skill in the art would have been motivated to include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine the patients whether is suffering from the side effects of ketogenic diet. Since ketogenic diet is known to have a certain portion of carbohydrate, fats and proteins, then adjusting the amounts of each to fit individual needs would be considered obvious as being within the purview of skilled artisan. Monitoring

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(determining) whether the patients still have the side effects or not is an integral part of therapy, which is obvious within the purview of the skilled artisan.

Claims 46 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marquie et al., Pentikainen et al., Poupon et al., Spasmo-canulase® Bitab®, and Krause et al. package insert as applied to claims 45, 47, 49-50, 52, and 54 -56 above, and further in view of Hydrocotyle (A Modern Herbal Home Page, 1995), Kang et al. (Archives of Physiology and Biochemistry, 1997;105(6):603-607), Pondimin monograph (PDR, 1996, page 2066-2067), and Keown et al. (WO 95/11034), references of record.

Marquie et al., Pentikainen et al., Poupon et al., and Spasmo-canulase® Bitab® package insert suggest the method of treating side effects of ketogenic diet by employing the herein claimed agents.

The references do not expressly teach the ketogenic diet side effects treating method employing also centella asiatica triterpene, selenium, yohimbine, phendimetrazine, and fenfluramine in the herein claimed amount.

Hydrocotyle teaches that centella asiatica is known to be a mild stimulant (See the Medicinal Action and Uses Section).

Kang et al. teaches that selenium is useful as lowering cholesterol level in subject taking high fat diet (See the abstract).

Pondimin monograph teaches fenfluramine is useful in increasing glucose utilization (see pharmacology Section).

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Keown et al. teaches sympathomimetic agents, such as yohimbine and phendimetrazine, as useful in increasing fat metabolism and lowering serum cholesterol level in the amount from about 0.001 to 99.90% (See particularly page 9, lines 8-16; also claim 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ all the herein claimed agents, in the herein claimed amount, into the method of treating the side effects of ketogenic diet.

One of ordinary skill in the art would have been motivated to employ all the herein claimed agents, in the herein claimed amount, into the method of treating the side effects of ketogenic diet. All the agents herein can help relieving one of the side effects of ketogenic diet: centella asiatica, which contains the triterpene, can be useful to treat fatigue since it is a mild stimulant; selenium is useful in treating hypercholesterolemia because it can lower the cholesterol level; fenfluramine is useful for hyperglycemia because it can increase the utilization of glucose and causing hypoglycemia; yohimbine and phendimetrazine are useful for hypercholesterolemia.

One of ordinary skill in the art would know that side effects of ketogenic diets include hypercholesterolemia, hyperglycemia, hyperuricemia, fatigue, change in mental status, nausea, and vomiting. Therefore, combining and employing two or more agents which are known to be useful to treat side effects of ketogenic diet individually into a single method useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. Furthermore, the optimization of result effect parameters (i.e., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

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(11) Response to Argument

Appellant's remarks in pages 12-13 of the Appeal Brief filed June 6, 2005 with regard to the presence of synergistic effect are unconvincing. Appellant further states, "Nobody has demonstrated a surprising synergistic effect of a composition ..." (See page 13 of the Brief). Examiner notes that no data was present to demonstrate the alleged unexpected benefits since no comparative data was shown. There is no evidence showing the combination of the herein claimed agents producing more than additive effects as comparing to the agents being administered alone. Therefore, unexpected or synergistic effects are not seen to be present herein.

Appellant's arguments in page 16 of the Appeal Brief filed June 6, 2005 averring the cited prior art's failure to teach the specific intended purpose of incorporating pancreatin IX F.U. are unconvincing. Examiner notes that the fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Appellant's arguments in page 17 of the Appeal Brief filed June 6, 2005 averring the cited prior art's failure to teach the herein claimed amounts are unconvincing. Absent evidence to the criticality of the herein claimed amounts, it is considered routine to one of ordinary skill in the art to adjust and optimize the amounts of the active. As anyone of ordinary skill in the art will appreciate, preferred dosages are merely exemplary and serve as useful guideposts for the physician. There are, however, many

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reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe infection would require a correspondingly higher dosage. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. For these and other self-evident reasons, it would have been obvious to have the dosage optimized.

Appellant's arguments in page 17-19 of the Appeal Brief filed June 6, 2005 averring the cited prior art's failure to provide motivation to combine the herein claimed agents into a single method of treating the side effects of ketogenic diet are unconvincing. Appellant citing *In re Bond*, 910 F.2d 831, 834; 15 U.S.P.Q. 2d 1566, 1568 (Fed. Cir. 1990) stating that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absents some teachings or suggestion or incentive to combine them. Examiner notes that the herein claimed agents, except for Spasmo-canulase[®] Bitab[®], are known to be useful in treating various side effects of ketogenic diet, as discussed in the above section. Therefore, employing them together for the very same purpose, i.e., treating side effects of ketogenic diet, is considered obvious (See *In re Kerkhoven supra*). Furthermore, Spasmo-canulase[®] Bitab[®], which contains pancreatin and sodium dehydrocholate, is known for relieving abdominal cramps associated with flatulence. Since flatulence and abdominal cramps are the common side effects of metformin, employing Spasmo-canulase[®] Bitab[®] would be reasonably expected to be effective in relieving the side effects of metformin and be useful in the herein claimed method, which utilize metformin.

Appellant's arguments in pages 19-20 of the Appeal Brief filed June 6, 2005 averring the Examiner as being inappropriately combine the cited prior arts' teachings based on *Kerkhoven* are unconvincing. Examiner notes that the court's analysis in *Geiger* was based on the notion of "non-analogous" art and the combining of elements from different (i.e., non-analogous) arts. The case at bar is therefore distinguishable from *Geiger*. Here, all the elements, except for Spasmo-canulase[®] Bitab[®], are known to be useful in treating various side effects of ketogenic diet in the pharmaceutical arts. The idea of combining them flows logically from their having been individually taught in the prior art, *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Appellant's arguments in page 20-21 of the Appeal Brief filed June 6, 2005 averring the Examiner applying "obvious to try" standard in the rejection under 35 USC 103(a) is unconvincing. Examiner notes that Appellant's invention is directed to a method of treating side effects of ketogenic diet with the herein claimed agents. The reasonable expectation of success is present in the teachings of the cited prior arts and thus, the instant rejection does not apply "obvious to try" standard. The herein claimed agents are known in the art to reduce cholesterol levels, concomitantly employing them together in a method of performing the same function would then be reasonably expected to be effective, at least additive effect would be expected.

Appellant's arguments in page 22-23 of the Appeal Brief filed June 6, 2005 averring the cited prior arts' failure to provide motivation to combine the herein claimed agents are not convincing. As discussed above and in the previous office action, the herein claimed agents are known to be useful as treating the side effects of ketogenic

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diet. Therefore, possessing the teachings of the cited prior art, one of ordinary skill in the art would have been reasonably expected to concomitantly employ the herein claimed agents together in a single method of treating the very same condition.

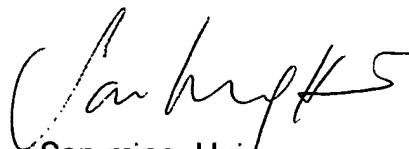
Appellant's invention define no more than a method of employing a collection of agents that are useful for treating side effects of ketogenic diet together in a same method to employ the same. Appellant further fails to provide unexpected result, the claims therefore, are considered to be properly rejected under 35 USC 103(a).

For the above reasons, it is believed that the rejections should be sustained.

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Respectfully submitted,



San-ming Hui
Primary Examiner
Art Unit 1617

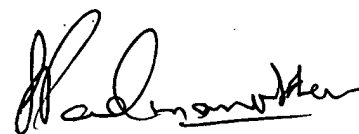
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